REMARKS

Claims 7-22 have been cancelled and new claims 23-44 have been added. Upon entry of the amendment above, claims 23-44 will be pending in this application. Reconsideration of the merits of the application in light of the above amendment and the remarks below is respectfully requested.

No new matter has been added as a result of the addition of the new claims. New claims 23-44 have been reworded to recite inhibition of HIV replication rather than treatment and correspond in scope to cancelled claims 7-22. The changed language to "inhibition of HIV replication" more closely reflects the data presented in the present application.

The inhibition recited in the new claims includes treatment of resistant HIV, as inhibition of HIV replication would occur if a person infected with HIV were administered either of the compounds recited in the present claims.

Rejection under 35 USC 103

Claims 7-22 have been rejected under 35 USC 103 as allegedly being unpatentable over Lind et al. Applicants traverse the rejection to the extent that it is applied to new claims 23-44.

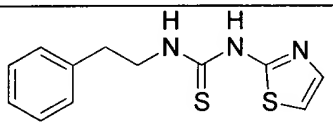
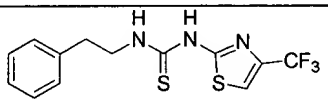
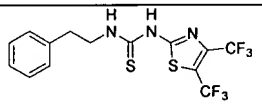
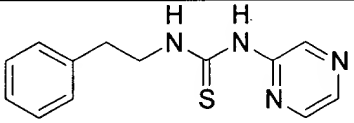
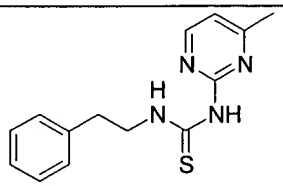
I. OBVIOUS TO TRY IS NOT OBVIOUSNESS UNDER 35 USC §103

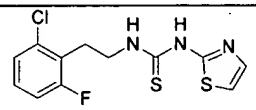
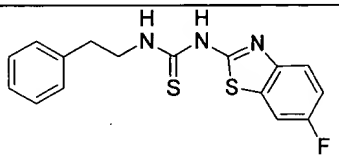
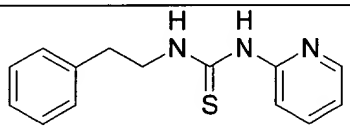
The Examiner argues that it would be obvious, based on the teachings of Lind et al., to try to treat resistant HIV using the compounds recited in the present claims. However, "obvious to try" is not the same as "obviousness". In re Goodwin, 576 F.2d 375, 377 (CCPA 1978), aff'd, 599 F.2d 1061 (CCPA 1979).

The Examiner is, in essence, asserting that it would be obvious to go through the millions of compounds disclosed by Lind et al. to reach one of the two compounds recited in the present claims. Clearly, this would not be an acceptable approach for treating an AIDS patient not responding to conventional therapy.

There is nothing in Lind et al. that would suggest that either of the two compounds recited in the present claims would be useful for treating or inhibiting resistant HIV. In this regard, the Examiner points to Example 4 on page 158 of Lind et

al, where the "core" (as termed by the Examiner) compound of the compounds recited in the present claims is disclosed. However, as Applicants stated their January 22,2002 Response, the activity of this "core" compound in Example 4 of Lind et al. is considerably less than the activity of other compounds having a different core (see Tables A1-A3 at pages 128-142of Lind et al.). Reproduced below is a table summarizing the results presented in Lind et al that Applicants previously submitted in their January 22, 2002 Response.

Test Compound	% Inhibition of HIV-RT at below compound concentration			
	100 ug/ml	10 ug/ml	1 ug/ml	0.1 ug/ml
 1-Phenethyl-3-thiazol-2-yl-thiourea	-	100	100	2
 1-Phenethyl-3-(4-trifluoromethyl-thiazol-2-yl)-thiourea	66	24	100	-
 1-(4,5-Bis-trifluoromethyl-thiazol-2-yl)-3-phenethyl-thiourea	99	85	71	-
 1-Phenethyl-3-pyrazin-2-yl-thiourea	100	100	4	-
 1-(4-Methyl-pyrimidin-2-yl)-3-phenethyl-thiourea	100	64	42	-

Test Compound	% Inhibition of HIV-RT at below compound concentration			
	100 ug/ml	10 ug/ml	1 ug/ml	0.1 ug/ml
 1-[2-(2-Chloro-6-fluoro-phenyl)-ethyl]-3-thiazol-2-yl-thiourea	100	100	100	-
 1-(6-Fluoro-benzothiazol-2-yl)-3-phenethyl-thiourea	100	100	100	-
 1-Phenethyl-3-pyridin-2-yl-thiourea	**6**	**2**	**0**	-

As shown from the table above, the data disclosed in Lind et al. indicates that 1-Phenethyl-3-pyridin-2-yl-thiourea, the "core" of the compounds recited in the present claims, is considerably less effective than other compounds having different cores.

Applicants assert that a physician treating an AIDS patient not responding to conventional therapy would not rationally select derivatives of a core compound having such relatively low activity. Rather, one would rationally be motivated to select the compounds disclosed in Lind et al. as having the best activity against non-resistant HIV, or structurally similar compounds.

A person of skill in the art, in attempting to treat or inhibit resistant HIV, would not, in light of Lind et al., logically arrive at either of the two compounds recited in the present claims for use in treating or inhibiting resistant HIV. While it may be obvious for a physician to select a different therapeutic compound when faced with a patient unresponsive to conventional therapy, there is nothing in Lind et al. that would direct or even suggest to a physician to try one of the two compounds recited in the present claims.

II. LIND ET AL. DO NOT SUGGEST A REASONABLE EXPECTATION OF SUCCESS

To establish obviousness under 35 USC 103, some reasonable expectation of success must be gleaned from the prior art.

> "Where claimed subject matter has been rejected as obvious ... a proper analysis under § 103 requires, inter alia, consideration of ... whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success."

In re Vaeck (1991), .947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991); see also *In re Dow Chemical Co.*, 837 F.2d 469,473, 5 USPQ2d 1529, (Fed. Cir., 1988); *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1209, 18 U.S.P.Q.2d) 1016, (CAFC 1991).

The Examiner fails to show that one would have any reasonable expectation of success, based on the disclosure of Lind et al., in using one of the two compounds recited in the present claims in inhibiting resistant HIV. As stated above, the "core" compound disclosed in Lind et al. was considerably less effective than other compounds in inhibiting non-resistant HIV. Lind et al. provide no suggestion that the compounds recited in the present claims would have superior properties against resistant HIV. In fact, Lind et al. do not discuss the efficacy of any of the millions of disclosed compounds against any resistant strain of HIV.

Resistant HIV strains are different from the non-resistant HIV disclosed in Lind et al. Resistant strains develop mechanisms, typically gene mutations, which render them resistant to the inhibitory effects of compounds. Often, HIV strains can develop resistance to many classes of inhibitory compounds. Such strains are termed multi-drug resistant HIV. Resistant HIV, because of their resistance mechanisms, are more difficult to treat than non-resistant strains. In fact, the main difficulty in HIV therapy is the rapid emergence of drug resistant strains of the virus. Tanuri et al., Antimicrobial Agents and Chemotherapy, 43(2): 253-358, 1999 at 253.

As stated in Applicants' January 22, 2002 Response, Lind et al. disclose non-resistant strains of HIV-1. These strains have not developed any resistance mechanisms

and are relatively easy to treat. Lind et al. do not disclose resistant HIV strain, nor do they suggest that the compounds recited in the present claims would have superior properties against resistant HIV. Based on the difficulties of treating resistant HIV and the fact that Lind et al. teach that the "core" compound of the compounds recited in the present claims exhibit relatively low activity compared to other compounds having a different core, one would have no expectation of success in using the claimed compounds for inhibiting resistant HIV.

III. APPLICANTS HAVE SHOWN UNEXPECTED RESULTS

Nothing in Lind et al. suggests that either of the two compounds recited in the present claims would be effective against drug resistant HIV. As indicated above, drug resistant strains of HIV are more difficult to treat than non-resistant HIV. DDE236 and DDE240, which are the compounds recited in the present claims, are quite potent against various resistant HIV strains, as shown in Table 2 at page 12 of the specification of the present application. The fact that these compounds have such potency is quite surprising.

Further, nothing in Lind et al. suggests that that the compounds recited in the present claims, which are non-nucleoside inhibitors (NNIs) of reverse transcriptase, would be effective against strains of HIV resistant to conventional NNIs. As shown in Table 2 at page 12 of the present application, the compounds recited in the present claims (DDE236 and DDE 240) are effective against HIV resistant to conventional NNIs. For example, Nevirapine and Delavirdine, which are conventional NNIs, were shown to be substantially ineffective against strains of HIV having a mutation at amino acid 181 of reverse transcriptase. However, DDE236 and DDE240 were much more effective against such resistant HIV (see Table 2 at page 12 of the present specification). In addition, DDE236 and DDE240 were 80-1000 times more potent than Nevirapine and Delavirdine against the HIV multi-drug resistant strain, RT-MDR. These results are surprising and certainly unexpected.

For the Examiner's convenience, relevant portions of Table 2 of the present application is reproduced below.

RT Inhibitors	RRT (μM)	HTLV IIIB WT	RT-MDR (74V, 41L, 106A, 215Y)	A17 (Y181C)	A17 variant (Y181C, K103N)
		IC50 p24 (μM)	IC50 p24 (μM)	IC50 p24 (μM)	IC50 p24 (μM)
DDE236	0.1	<0.001	0.005	0.1	11
DDE240	0.6	<0.001	0.005	0.2	41
Delavirdine	1.5	0.009	0.4	50	>100
Nevirapine	23	0.034	5	>100	>100

N.D.= not determined; WT=wild type.

As can be seen by the above reproduction of portions of Applicant's Table 2, Applicants have show that the compounds recited in the claims (DDE236 and DDE240) are effective against HIV strains having reverse transcriptase mutations in various positions. Again, this is surprising and unexpected as the conventional NNIs are relatively ineffective against these mutations.

IV. GENERIC CLAIM 27 OF LIND ET AL. DOES NOT CURE SPECULATIVE NATURE OF EXAMINER'S POSITION

The Examiner pointed to claim 27 of Lind et al. to assert that the nature of the rejection is not hypothetical or speculative. . However, there are thousands, if not millions, of permutations of potential compounds disclosed within claim 27 of Lind et al. Accordingly, claim 27 hardly limits the speculative nature of the Examiner's position. While claim 27 of Lind et al. does generically include the two compounds recited in the claims of the present application, there is nothing special about the claim that would direct one to use one of the two specifically recited compounds of the claims of the present application. More importantly, there is no suggestion in claim 27, or anywhere in Lind et al., that these two compounds would be useful for treating or inhibiting drug resistant HIV.

V. THE EXAMINER'S RELIANCE ON *IN RE SWINEHART* IS MISPLACED

The Examiner asserts that elucidation of the mode of action does not impart patentable moment to otherwise old and obvious subject matter, citing *In re Swinehart.* However, *In re Swinehart* stands for the proposition that claims to compounds reciting previously unknown functional properties are not patentable over prior art disclosing the compound itself. However, Applicants are claiming a new use of a known compound, not a compound having functional properties. It is well-established patent law that new uses of old compounds are patentable. For example, 35 U.S.C. 100(b) defines "process" as including "a new use of a known ... composition of matter", while 35 U.S.C 101 explicitly states that "[w]hoever invents or discovers any new and useful process ... may obtain a patent therefor..." Accordingly, a new use of a known compound is patentable. The courts have also agreed that a new and unobvious use of a known composition is patentable. See, e.g, *Rhom & Hass Co. v. Roberts Chemicals*, 245 F.2d 693, 113 USPQ 423 (4th Cir. 1957); *In re Schoenwald*, 964 F.2d 1122, 22 USPQ 1671 (Fed. Cir. 1992); *Loctite Corp. v. Ultraseal Ltd.*, 781 F.2d 861, 875, 228 USPQ 90, 99 (Fed. Cir. 1985); *In re Shetty*, 566 F.2d 81, 83, 195 USPQ 753, 754 (CCPA 1977).

VI. APPLICANTS ULTIMATE UTILITY IS NEW AND UNOBVIOUS

The Examiner asserted that the ultimate utility of the claimed invention is old and well known and described in the prior art. Apparently, the Examiner neither recognizes the differences between drug-resistant HIV and the HIV disclosed in Lind et al., nor recognizes the difficulties associated with treating or inhibiting drug-resistant HIV.

Applicants respectfully assert that the use of the compounds recited in the present claims to inhibit drug-resistant strains of HIV is new and non-obvious over the art cited by the Examiner. High replication rates of HIV unfortunately lead to genetic variants, which could result in drug resistance, especially when selective pressure is introduced in the form of drug treatment. In fact, the main difficulty with current treatment of HIV is the development of drug resistance of the virus. Tanuri et al., Antimicrobial Agents and Chemotherapy, 43(2): 253-358, 1999 at 253. Finding compounds useful for treating

resistant HIV is no easy task. This is particularly true of compounds that exhibit improved ability to inhibit known drug resistant strains of HIV. Applicants have found that the two compounds recited in the present claims, DDE 236 and DDE 240, exhibit such improved ability. Nothing in the art cited by the Examiner (Lind et al.) teaches or suggests that DDE 236 and DDE 240 would have such properties. Case law and statute agree that Applicants should be entitled to patent claims directed to this new and unobvious use of the known compounds.

In light of the above remarks, withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the above, Applicant respectfully requests withdrawal of the rejections and allowance of the claims. Prompt passage to issue is earnestly solicited. Should the Examiner feel a telephone interview would be helpful in advancing this case to allowance, Applicant invites the Examiner to contact their representative at the number listed below.

Respectfully submitted,

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Dated: 24 Sept 2002

By: Keith Campbell
Keith Campbell
Reg. No. 46,597

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	UCKUN	Examiner:	R. TRAVERS
Serial No.:	09/272,821	Group Art Unit:	1617
Filed:	MARCH 20, 1999	Docket No.:	12152.55US01
Title:	NNI FOR TREATMENT OF MULTIDRUG RESISTANT HIV		

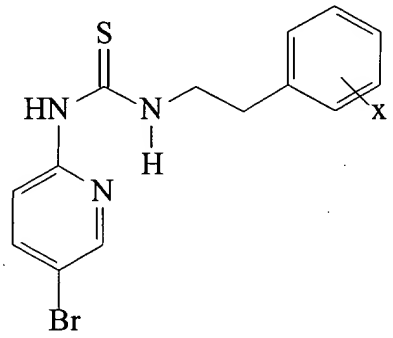
Version with Markings to Show Changes Made

IN THE CLAIMS

Claims 7-22 were cancelled and add new claims 23-44 were added as follows.

23. (New) A method for inhibiting replication of a virus of an HIV strain that is resistant to a chemotherapeutic agent, the method comprising:
contacting the resistant virus with an amount of a compound effective to inhibit replication of the virus,

wherein the compound is of the formula:



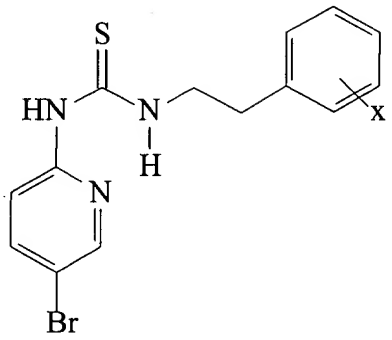
wherein x is: 2,5-OMe or *o*-F.

24. (New) The method of claim 23, wherein the chemotherapeutic agent is Delavirdine, Nevirapine, Efavirenz, Trovirdine, AZT, or MKC-442.

25. (New) A method for inhibiting replication of an HIV having a mutation of an amino acid at position 106 or 183 of reverse transcriptase, the method comprising:

contacting the HIV with an amount of a compound effective to inhibit replication of the HIV,

wherein the compound is of the formula:

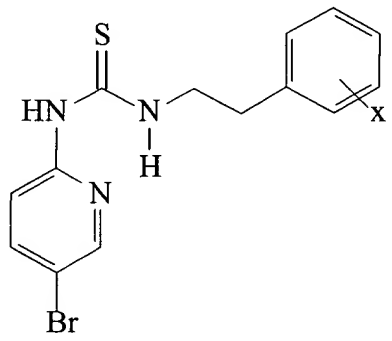


wherein x is: 2,5-OMe or *o*-F.

26. (New) A method for inhibiting replication of an HIV having one or more of the following amino acid substitutions in reverse transcriptase : L100I, K103N, V106A, E138K, Y181C, or Y188H; the method comprising:

contacting the HIV with an amount of a compound effective to inhibit replication of the HIV,

wherein the compound is of the formula:

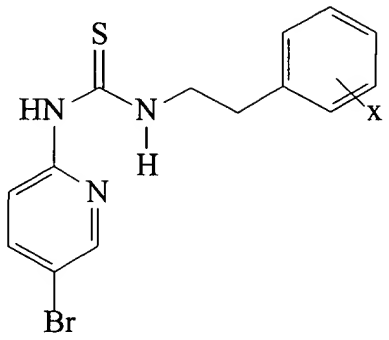


wherein x is: 2,5-OMe or *o*-F.

27. (New) A method for inhibiting replication of a virus of an HIV strain that is resistant to a non-nucleoside inhibitor-resistant strain of HIV; the method comprising

contacting the resistant virus with an amount of a compound effective to inhibit replication of the virus,

wherein the compound is of the formula:

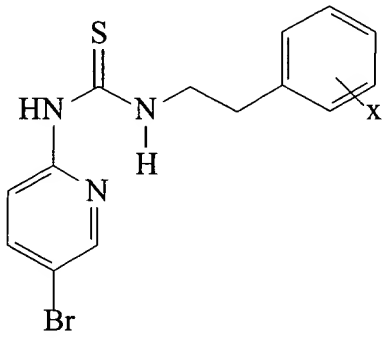


wherein x is: 2,5-OMe or *o*-F.

28. (New) A method of inhibiting replication of a virus of an HIV strain selected from the group consisting of RT-MDR, HIV A17, and HIV A17 variant; the method comprising:

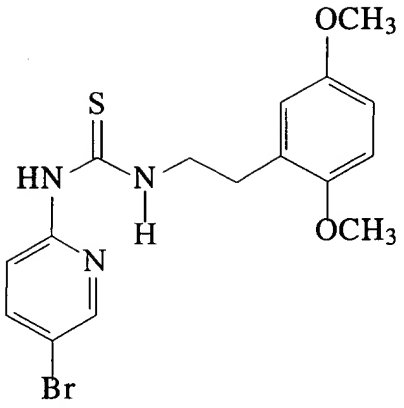
contacting the virus with an amount of a compound effective to inhibit replication of the virus

wherein the compound is of the formula:

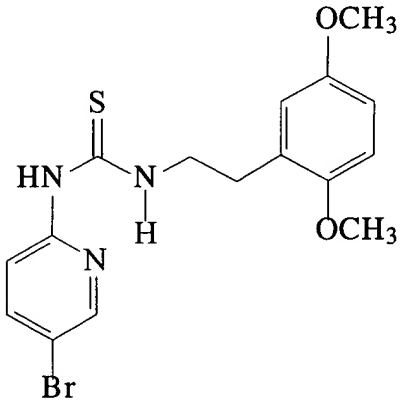


wherein x is: 2,5-OMe or *o*-F.

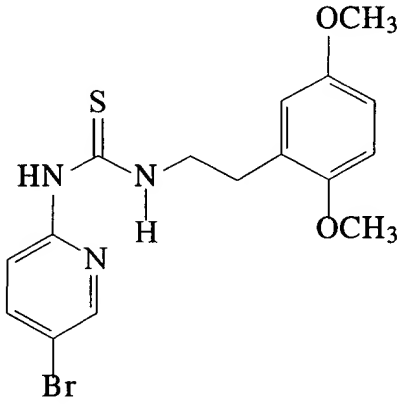
29. (New) The method of claim 23, wherein the compound is



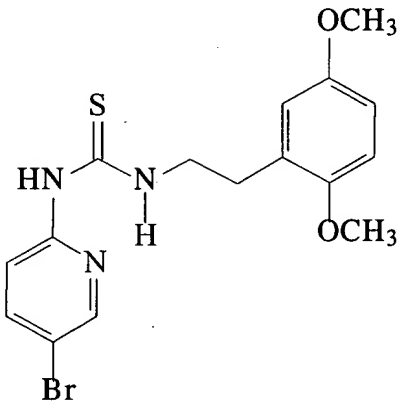
30. (New) The method of claim 25, wherein the compound is



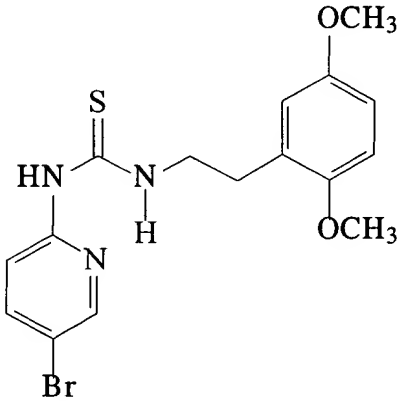
31. (New) The method of claim 26, wherein said compound is



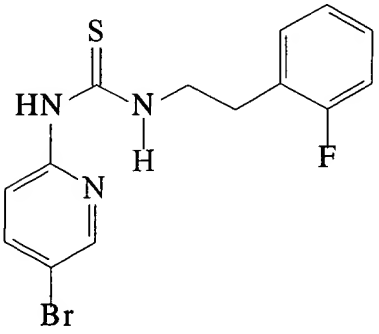
32. (New) The method of claim 27, wherein the compound is



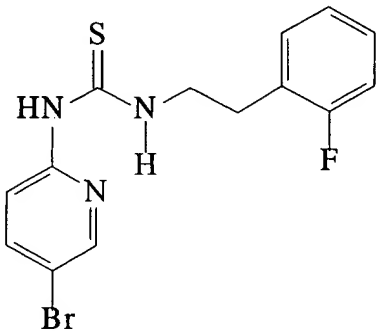
33. (New) The method of claim 28, wherein the compound is



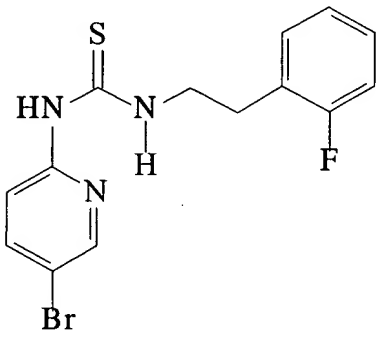
34. (New) The method of claim 23, wherein said compound is



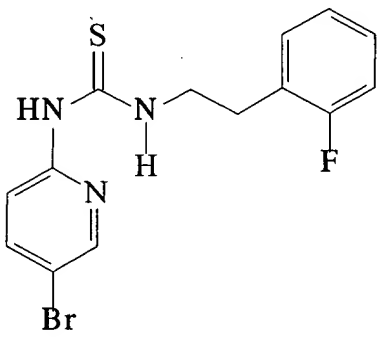
35. (New) The method of claim 25, wherein the compound is



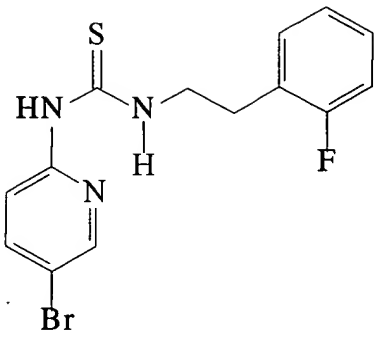
36. (New) The method of claim 26, wherein the compound is



37. (New) The method of claim 27, wherein the compound is



38. (New) The method of claim 28, wherein the compound is



39. (New) The method of claim 23, wherein the replication of the virus is inhibited within a human peripheral blood mononuclear cell.

40. (New) The method of claim 24, wherein the replication of the virus is inhibited within a human peripheral blood mononuclear cell.

41. (New) The method of claim 25, wherein the replication of the HIV is inhibited within a human peripheral blood mononuclear cell.

42. (New) The method of claim 26, wherein the replication of the HIV is inhibited within a human peripheral blood mononuclear cell.

43. (New) The method of claim 27, wherein the replication of the virus is inhibited within a human peripheral blood mononuclear cell.

44. (New) The method of claim 28, wherein the replication of the virus is inhibited within a human peripheral blood mononuclear cell.